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Clinical and Roentgenographic Findings in a Patient With Primordial Microcephalic Dwarfism Type Caroline Crachami

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We describe a patient with primordial microcephalic dwarfism with severe intrauterine growth retardation and severe and progressive postnatal deficit in length, weight and head circumference. The patient was extroverted and sociable but mildly mentally retarded. He had marked delay of bone maturation and an enlargement of the sella turcica. This child and two previously reported patients [Boscherini et al., Eur J Pediatr 137:237–242, 1981] have many characteristics in common with Caroline Crachami, the famous "Sicilian dwarf." We think that these patients belong to a separate category of microcephalic primordial dwarfism. © 1996 Wiley-Liss, Inc.

KEY WORDS: microcephalic primordial dwarfism, osteodysplastic primordial dwarfism type III, Seckel syndrome, intrauterine growth retardation

INTRODUCTION

In 1960, Seckel identified a syndrome within the heterogeneous group of children or adults with relative proportionate primordial dwarfism and microcephaly, a condition named "Seckel syndrome." According to Majewski and Goecke [1982], who used strict diagnostic criteria, only 17 out of approximately 60 patients described up to 1982 could be considered true Seckel syndrome cases. More recently, Majewski [1992] reported on two cases with severe pre- and postnatal growth retardation, microcephaly and distinctive face, different from that of children with Seckel syndrome, pseudosenile appearance, severe mental retardation, knee contracture, flat and enlarged sella turcica, generalized osteoporosis, concave impression of vertebral bodies, cone-shaped phalangeal epiphyses, and thin diaphyses with medullary stenosis. Majewski thought that these two patients, along with six other patients described previously [Toudic et al., 1977; Neumann and Karte, 1982; Boscherini et al., 1981; Seckel, 1960] represent a new type of primordial microcephalic dwarfism which he named osteodysplastic primordial dwarfism type III (OPD III) [Majewski, 1992].

One patient included by Majewski, as an example of this new syndrome, is Caroline Crachami, the famous "Sicilian dwarf," who had been reported previously in Seckel's monograph [Seckel, 1960]. However, on the basis of further data collected from old portraits, the autopsy report, and other sources, Bondeson [1992] suggested that Caroline Crachami might belong to a "hitherto undescribed subgroup of intrauterine growth retardation" having some manifestations in common with the patients described by Majewski [1992] but also showing considerable differences [Bondeson, 1993].

Here we describe a new case of primordial microcephalic dwarfism. The clinical and growth characteristics of this patient resemble those of Caroline Crachami and of two other patients described previously by some of us (Table I) [Boscherini et al., 1981].

CLINICAL REPORT

D.G., the only child of nonconsanguineous parents (Fig. 1), was born at term after a pregnancy complicated by a threatened miscarriage. Birth weight was 1,030 g, birth length and head circumference (OFC) were not reported. At 4 months, his weight was 1,700 g, at 9 months 2,380 g.

This child first came to our attention at 13 months (Fig. 1). At that time, weight was 3,030 g, OFC 35 cm, chest circumference 35 cm, length 52 cm (−8.9 S.D.). He presented with (Fig. 2): marked microsomia with a small head, hypoplastic mandible, steep forehead, beaked nose, small mouth with thin vermilion border of the upper lip and erupting lower incisors, apparently low-set ears, sparse hair, hypoelastic skin, scarce subcutaneous fat, and clinodactyly of the fifth fingers. Mild

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TABLE I. Clinical and Radiological Data on the Present Case (D.G.), Our Previous Observations (B1, B2), and Caroline Crachami (C.C.)[a]

Case	D.G.	B1	B2	C.C.
Psychomotor development	Mild delay	Mild delay	Mild delay	Mild delay
High-pitched voice	Yes	Yes	Yes	Yes
Sociable behavior	Yes	Yes	Yes	Yes
Poor subcutaneous tissue	Yes	Yes	Yes	Yes
Pseudosenile appearance	Yes	Yes	Yes	Yes
Characteristic face	Yes	Yes	Yes	Yes
Delayed bone age	Yes	Yes	Yes	?
Cone-shaped or sclerotic epiphyses	?	Yes	Yes	?
Osteodysplastic skeletal lesions	No	No	No	No
Long bones and ribs	Thin	Thin	Very thin	Very thin
Sella turcica volume	↑	↑	↑	?

[a]↑, enlarged.

psychomotor retardation was also present; he could not stay in an upright position and was able to utter only a few syllables. Results of routine laboratory tests were normal and chromosomes were normal (46,XY). After insulin stimulation test, GH plasma levels were normal (10 ng/ml). Oral glucose tolerance test (OGTT) and ECG were normal. X-ray examination showed marked delay in skeletal maturation. The skull showed abnormally short diameters for chronological age with evident microcephaly. The sella turcica was enlarged and very flat, with low posterior clinoid process (Fig. 3). Tridimensional measurement was not performed.

At 2 years, height was 55 cm (−9.3 S.D.), weight 3,650 g and weight/height ratio was approximately at the 10th centile. The appearance of the skeleton was unchanged.

At 3 years, length was 62 cm (−8.4 S.D.), weight 3,900 g, the ponderal deficit was 35% and OFC 37.5 cm. Head circumference was lower than 2 S.D. for height age. Scarcity of subcutaneous fat was still evident as well as mild psychomotor retardation. Height/weight ratio worsened in the first years of life. Bone age, determined according to Greulich and Pyle [1984], was 10 months; both hands showed accessory pseudo-epiphyses. Roentgenographs of the skeleton showed thin long bones and ribs, but no osteodysplastic lesions were

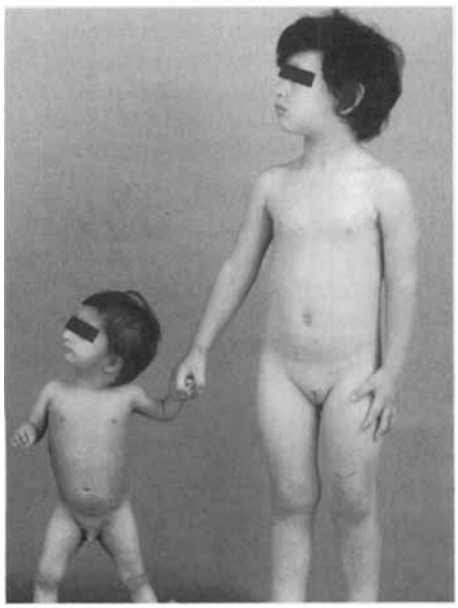

Fig. 1. The child D.G. compared with a normal peer of same age.

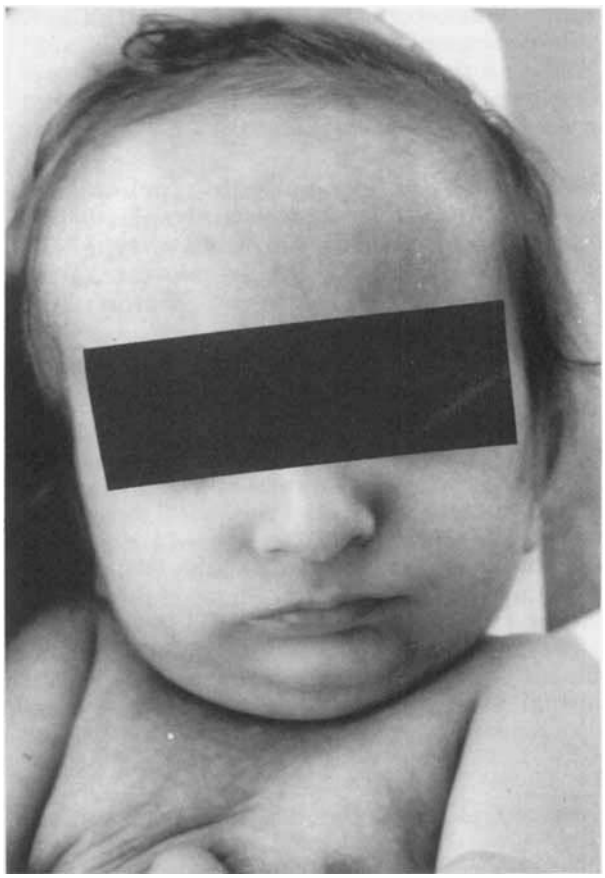

Fig. 2. The child D.G. Note facial appearance.

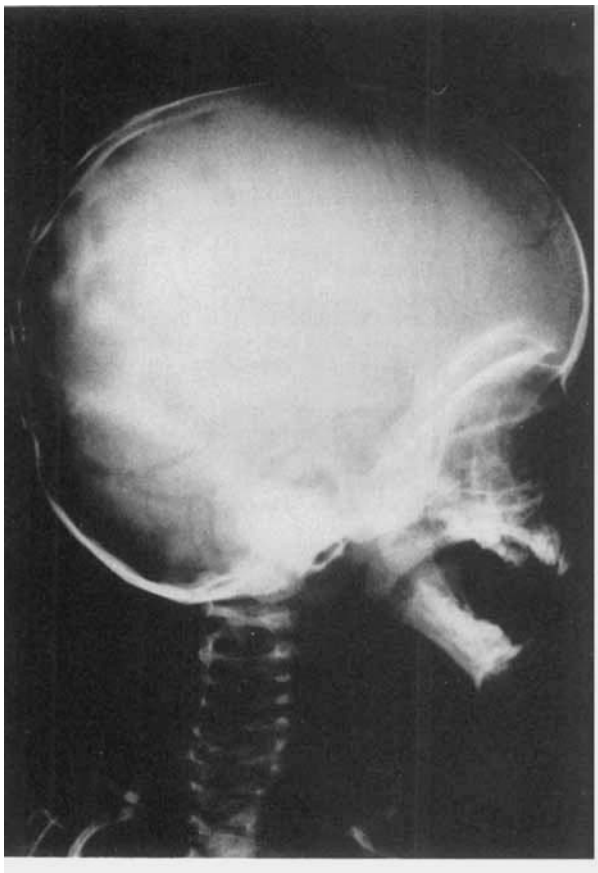

Fig. 3. Skull roentgenograph. Note the enlargement of the sella turcica.

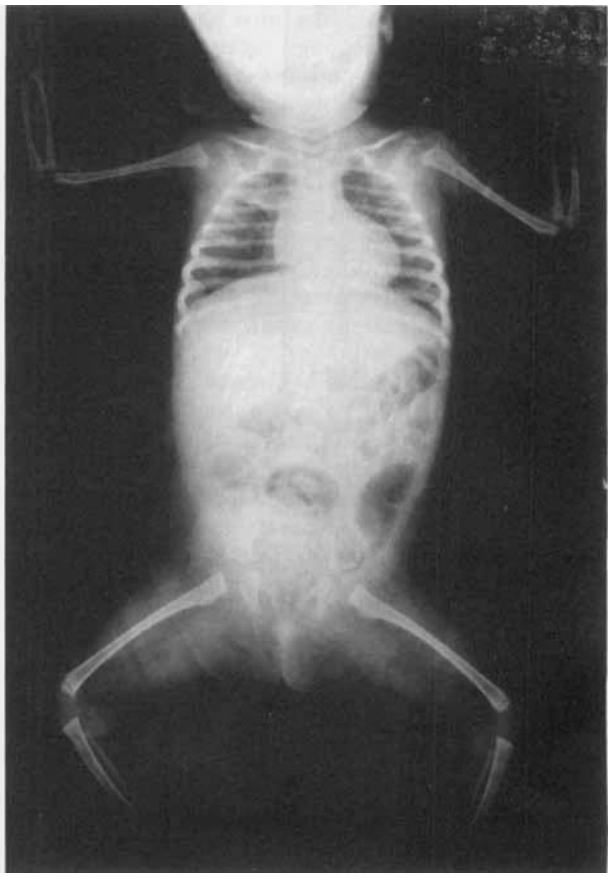

Fig. 4. Roentgenographs of the skeleton. Note thin long bones and ribs.

noted (Fig. 4). At 2 years, the child started walking. At 3 years, he could walk without support, and was able to use a few simple words. He was very sociable and loving, and despite his poorly developed vocabulary, comprehension was acceptable and he was able to establish reciprocal relationships with peers.

DISCUSSION

Our patient showed growth characteristics typical of primordial dwarfism with microcephaly, pseudosenile appearance, bird-like face, slightly decreased intelligence, sociable and extroverted behavior. The face was characterized by beaked nose, small mouth with thin vermillion border of the upper lip, small and hollow eyes, and micrognathia. Bone age was markedly delayed, but no osteodysplastic skeletal lesions were noted.

Due to the presence of intrauterine growth retardation and microcephaly, Seckel syndrome was considered a possible diagnosis. However, while intelligence is always severely retarded in Seckel syndrome, the intellectual development in our patient was more or nearly normal. Furthermore, in patients with Seckel syndrome, the forehead is receding, while in our patient the forehead was normal or mildly steep. Further characteristics present in our patient such as progeroid appearance, sociable behavior and increased size of the sella, do not fit with the Seckel syndrome.

On one hand, some of these phenotypic traits, especially the peculiar facies, pseudosenile appearance, scarcity of subcutaneous fat, increased size of the sella, were described by Majewski [1992] as component manifestations of OPD III. Nonetheless, there are some substantial differences. In our patient, birth weight was markedly reduced, while severe mental retardation, knee contracture, osteodysplastic lesions of the spine, marked osteoporosis and medullary stenosis of the long bones were not present. On the other hand, the auxological, clinical and roentgenographic characteristics are very similar to those described in two previous patients [Boscherini et al., 1981] included by Majewski [1992] into the OPD III. However, the differences between Majewski's patients and ours do not permit this inclusion. In fact, in those two patients, the intrauterine growth retardation was more severe, while mental retardation was mild and osteodysplastic skeletal lesions as well as articular contractures were absent. The child described in the present report and those previously reported by Boscherini et al. [1981] present many characteristics in common with Caroline Crachami, the patient first described by Seckel [1960] and subsequently by Bondeson [1992], and included by Majewski [1992] in OPD III. This girl presented, similar to our cases, the typical face, the pseudosenile appearance, mild mental retardation, sociable and extroverted behavior, a high-pitched voice and absence of osteodys-

plastic skeletal lesions. She also had an intrauterine growth retardation, although more severe than in our cases. Therefore, the hypothesis suggested by Bondeson [1992], that Caroline Crachami belongs to an undescribed subgroup of primordial microcephalic dwarfism with some characteristics different from Majewski's patient [Bondeson, 1993] is, in our opinion, confirmed. Furthermore, we think that our present patient, the two patients described previously by Boscherini et al. [1981], as well as Caroline Crachami, fall into the same subgroup, possibly representing a new syndrome to be named Caroline Crachami syndrome, as a tribute to the "Sicilian fairy."

Other previously published cases, such as those by Mann and Russell [1959] also could belong to this group. However, lack of clinical and, in particular, radiological findings, do not allow us to include these patients into this new syndrome with certainty. The patient described by Grossmann et al. [1954] had a pseudosenile appearance, and could also belong to this syndrome, even though he was severely mentally retarded. Fitch et al. [1970] described a patient with a form of bird-headed dwarfism with premature senility but his birth weight was normal. Growth hormone function assessed in these patients was normal, and growth hormone treatment undertaken in two children was not effective [Boscherini et al., 1981].

In conclusion, the patient described in the present report, along with our previous patients [Boscherini et al., 1981] and Caroline Crachami, seem to belong to a subgroup of microcephalic primordial dwarfism. Their peculiar auxological, clinical and radiological characteristics lead us to include them in a new and separate syndrome.

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